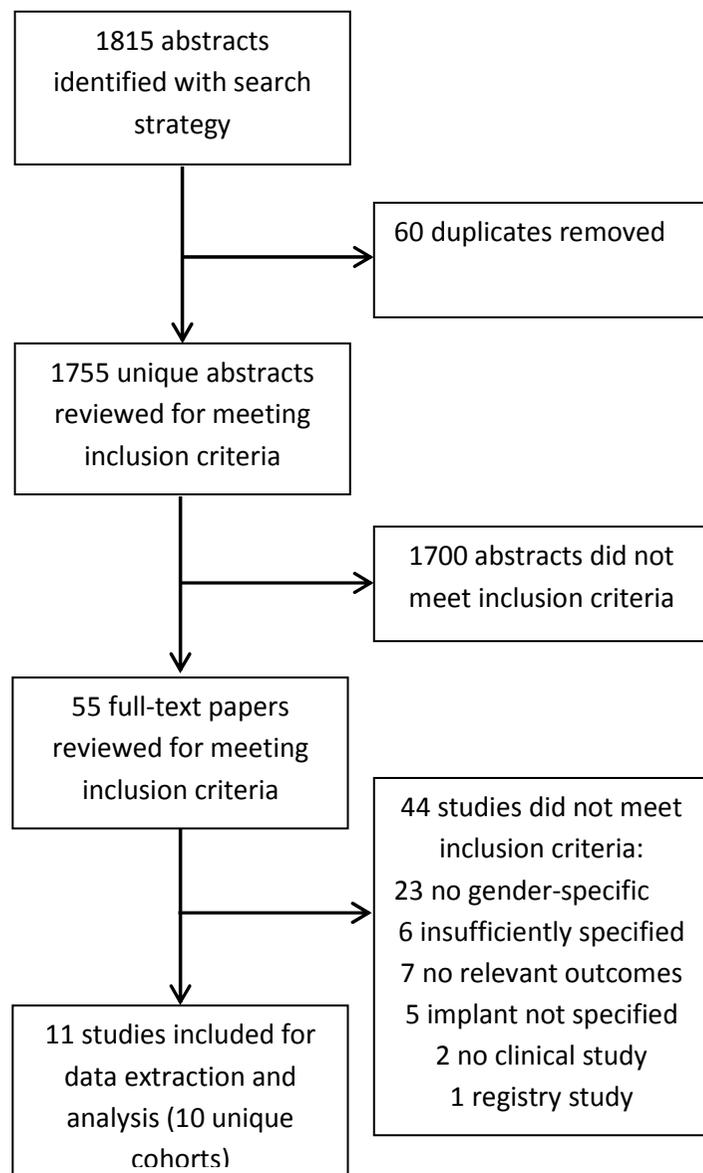


Appendix 6: Gender-specific total knee replacements

- Flow diagram of included studies
- Study details 1 (aspects of internal validity)
- Study details 2 (aspects of external validity)
- Study reported outcomes
- Forest plots
- Funnel plot
- References

Flow chart



Study details I (aspects of internal validity)

Study	Study design	Allocation method and concealment	Blinding (surgeons/ patients/ assessors)	Prospective collection and assessment	Sample size needs clearly defined?	Primary Outcome specified? (yes/no)	Intention-to-treat analysis? (yes/no)	Consecutive patients series? (yes/no)	Group comparability assessed?	Controlling for confounding?	Procedure period
Eggers, 2012	Retrospective comparison of successive consecutive cohorts	Time period, no concealment	NA	No	No	Yes (Range-of-motion)	NA	yes	Demographics and preoperative assessments	No	November 2005 - February 2008
Emerson, 2008	Retrospective comparison of successive consecutive cohorts	Time period and surgeon's preference, no concealment	NA	No	Yes (post-hoc)	Yes (F-E ROM, based on power calculation)	NA	yes	Demographics and preoperative assessments	Statistical analysis stratified by gender	NA
Kim (A), 2010	Randomized controlled trial in patients with bilateral TKA	Unit of randomization unclear, concealment by sealed envelope opened before skin incision	Unclear	Yes	Yes	Yes (dimensional fit, based on power calculation)	Unclear	Yes	Demographics and preoperative assessments	Randomized design, patient served as own control	Nov 2006 - Jan 2007
Kim (B), 2010	Randomized controlled trial in patients with bilateral TKA	Unit of randomization unclear, concealment by sealed envelope opened before skin incision	Patients, outcome assessors	Yes	Yes	Yes (satisfaction, based on power calculation)	Unclear	Yes	Demographics and preoperative assessments	Randomized design, patient served as own control	May 2006 - Oct 2006
Klein, 2011, Roth, 2013	Randomized controlled trial	Randomization method and concealment unclear	Patients	Yes	Yes	Yes	Unclear	Unclear	Demographics and preoperative assessments	Randomized design	April 2010 – July 2010
Singh, 2012	Randomized controlled trial in patients with	Unclear	Unclear	Yes	No	No	Unclear	Unclear	Age and BMI	Randomized design	August 2008 - July 2009

	bilateral TKA										
Song (A), 2012	Prospective cohort with successive designs in same knee	NA (successive application in same knee)	Patients	Yes	Yes	Yes (F-E ROM, based on power calculation)	NA	Unclear	NA	Patients served as their own control	April 2007 – July 2007
Song (B), 2012	Randomized controlled trial in patients with bilateral TKA	Randomization, method and concealment unclear	Patients	Yes	Yes	Yes (F-E ROM, based on power calculation)	Unclear	Yes	Demographics and preoperative assessments	Randomized design, patient served as own control	NA
Tanavalee, 2011	Prospective comparison within consecutive cohort	Surgeon's preference, no concealment	NA	Outcome assessments only	No	Unclear	NA	Yes	Demographics and preoperative assessments	None, despite group gender difference	March 2007 - December 2008
Thomsen, 2012	Randomized controlled trial in patients with bilateral TKA	Randomization by computer generated list, concealment unclear	Patients, outcome assessors	Yes	Yes	Yes ('feel' of knee, based on power calculation)	Unclear	Unclear	Demographics and preoperative assessments	Randomized design, patient served as own control	March 2008 - May 2010

NA = not available (not applicable or not provided)

Study	Study details II (aspects of external validity)										
	No. Of replacements (no. of patients)	Mean age (SD, range)	Female (%)	Osteo-arthriti s (%)	Mean length of FU (SD, Range)	Follow-up completion (%)	Prosthesis brands (new vs conventional)	Manufactu rer	Site, surgeon	Hospital setting (designer/ university/ general)	Continent (country)
Eggers, 2012	194 (159)	68.1 (NA,NA)	100	NA	1.0 (NA, NA)	40.2	Gender-specific NexGen LPS/CR-Flex <i>versus</i> standard NexGen LPS CR	Zimmer	Single center, single surgeon	General	North America (US)
Emerson, 2008	NA (395)	64.8 (NA,NA)	49.6	98.7	0.5	NA	Vanguard CR	Biomet Inc.	Single center, single surgeon	General	North America (US)
Kim (A), 2010	176 (88)	69.7 (6.8, 51 - 86)	100	NA	2.1 (2.0 - 2.3)	96.6	Gender-specific NexGen LPS-Flex <i>versus</i> standard NexGen LPS-Flex	Zimmer	Single center, single surgeon	University	Asia (South Korea)
Kim (B), 2010	292 (146)	71.2 (NA, 51 - 82)	100	100	3.25 (NA, 3.1 - 3.5)	94.5	Gender-specific NexGen CR-Flex <i>versus</i> standard NexGen CR-Flex	Zimmer	Single center, single surgeon	University	Asia (South Korea)
Klein, 2011 Roth, 2013	80 (80)	68.2 (7.7, 47-87)	100	100	6 weeks	NA	Gender-specific NexGen LPS Flex <i>versus</i> NexGen LPS Flex	Zimmer	Single center, single surgeon	general	Europe (Germany)
Singh, 2012	200 (100)	66.4 (5, 60-80)	100	100	2.1 (1.6- 2.5)	100	Gender-specific NexGen LPS-Flex <i>versus</i> standard NexGen LPS	Zimmer	Single center, unclear	General	Asia (India)
Song (A), 2012	80 (40)	68.0 (NA, 52 - 81)	100	100	0 (intra-operative only)	100	Gender-specific NexGen CR-Flex <i>versus</i> standard NexGen CR-Flex	Zimmer	Single center, single surgeon	University	Asia (South Korea)
Song (B), 2012	100 (50)	68.8 (NA, 53 - 82)	100	100	2.63 (2.0 - 3.0)	92	Gender-specific NexGen CR-Flex <i>versus</i> standard NexGen CR-Flex	Zimmer	Single center, single surgeon	University	Asia (South Korea)
Tanavalee, 2011	314 (314)	70 (NA, 54 - 86)	84.4	100	2.42 (1.4 - 3.1)	95.2	Gender-specific NexGen LPS-Flex <i>versus</i> standard NexGen LPS-Flex	Zimmer	Single center, single surgeon	University	Asia (Thailand)
Thomsen, 2012	48 (24)	66 (NA, 49 - 85)	100	100	1.0 (NA, NA)	100	Gender-specific NexGen LPS-Flex <i>versus</i> standard	Zimmer	Single center, single surgeon	University	Europe (Denmark)

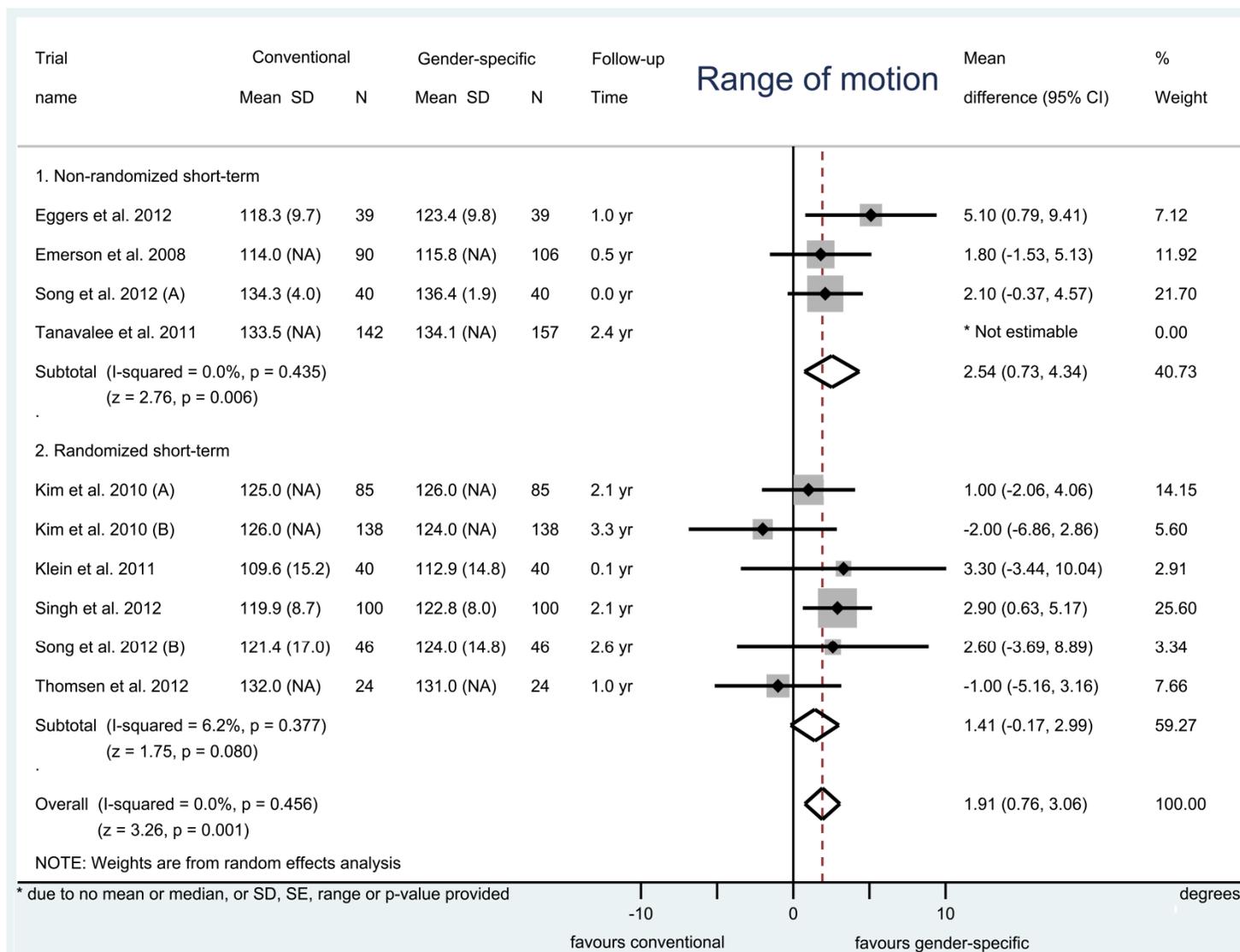
NA = not available (not applicable or not provided)

Study	Quality	Outcome	Flexion–extension (mean, SD / range)		Knee Society Score (mean, SD / range)		WOMAC (mean, SD / range)		Satisfaction (mean, SD / range)		Preference (count, proportion)		
			Gender	Standard	Gender	Standard	Gender	Standard	Gender	Standard	Gender	Standard	None
Eggers, 2012	Low	Preoperative	102.7 (9.5)	107.5 (11.5)	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Postoperative	123.4 (9.8)	118.3 * (9.7)	NA	NA	NA	NA	NA	NA	NA	NA	NA
Emerson, 2008	Low to moderate	Preoperative	114.0	109.6	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Postoperative	115.8 (77-135)	114.0 (85-132)	93.3 (60-100)	93.3 (65-100)	NA	NA	NA	NA	NA	NA	NA
Kim (A), 2010	Moderate to high	Preoperative	123 (85-150)	120 (58-150)	34.4 (7-62)	31.2 (0-55)	66.8 (29-94)	67.9 (31-96)	NA	NA	NA	NA	NA
		Postoperative	126 (85-140)	125 (80-140)	96.5 (83-100)	95.5 (84-100)	35.7 (5-61)	36.6 (4-69)	8.1 (1.9)	8.3 (1.7)	6 (7%)	8 (9%)	71 (84%)
Kim (B), 2010	High	Preoperative	127 (100-150)	123 (80-150)	39.8 (10-70)	35.3 (0-50)	NA	56.3 (26-89)	NA	NA	NA	NA	NA
		Postoperative	124 (85-140)	126 (85-140)	93 (70-100)	94 (70-100)	NA	26.4 (0-76)	7.9 (2.1)	8.1 (1.9)	14 (10.1%)	12 (8.7%)	112 (81.1%)
Klein, 2011 Roth, 2013	Moderate	Preoperative	114.2 (15.2)	111.6 (19.7)	43.2 (13.7)	41.3 (11.6)	138.5 (47.3)	152.2 (33.5)	NA	NA	NA	NA	NA
		Postoperative	112.9 (14.8)	109.6 (15.2)	85.6 (14.4)	77.8 * (16.8)	43.2 (29.5)	43.8 (29.7)	NA	NA	NA	NA	NA
Singh, 2012	Moderate	Preoperative	111.7 (13.5)	110.5 (13.7)	34.2 (11.5)	36.3 (13.4)	NA	NA	NA	NA	NA	NA	NA
		Postoperative	122.8 (8.0)	119.9 * (8.7)	94.9 (4.7)	95.8 (3.6)	NA	NA	NA	NA	NA	NA	NA
Song (A), 2012	Moderate	Preoperative	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Postoperative	136.4 (1.9)	134.3 (4.0)	NA	NA	NA	NA	NA	NA	NA	NA	NA
Song (B),	Moderate	Preoperative	120.4	121.8	NA	NA	69.6	66.2	NA	NA	NA	NA	NA

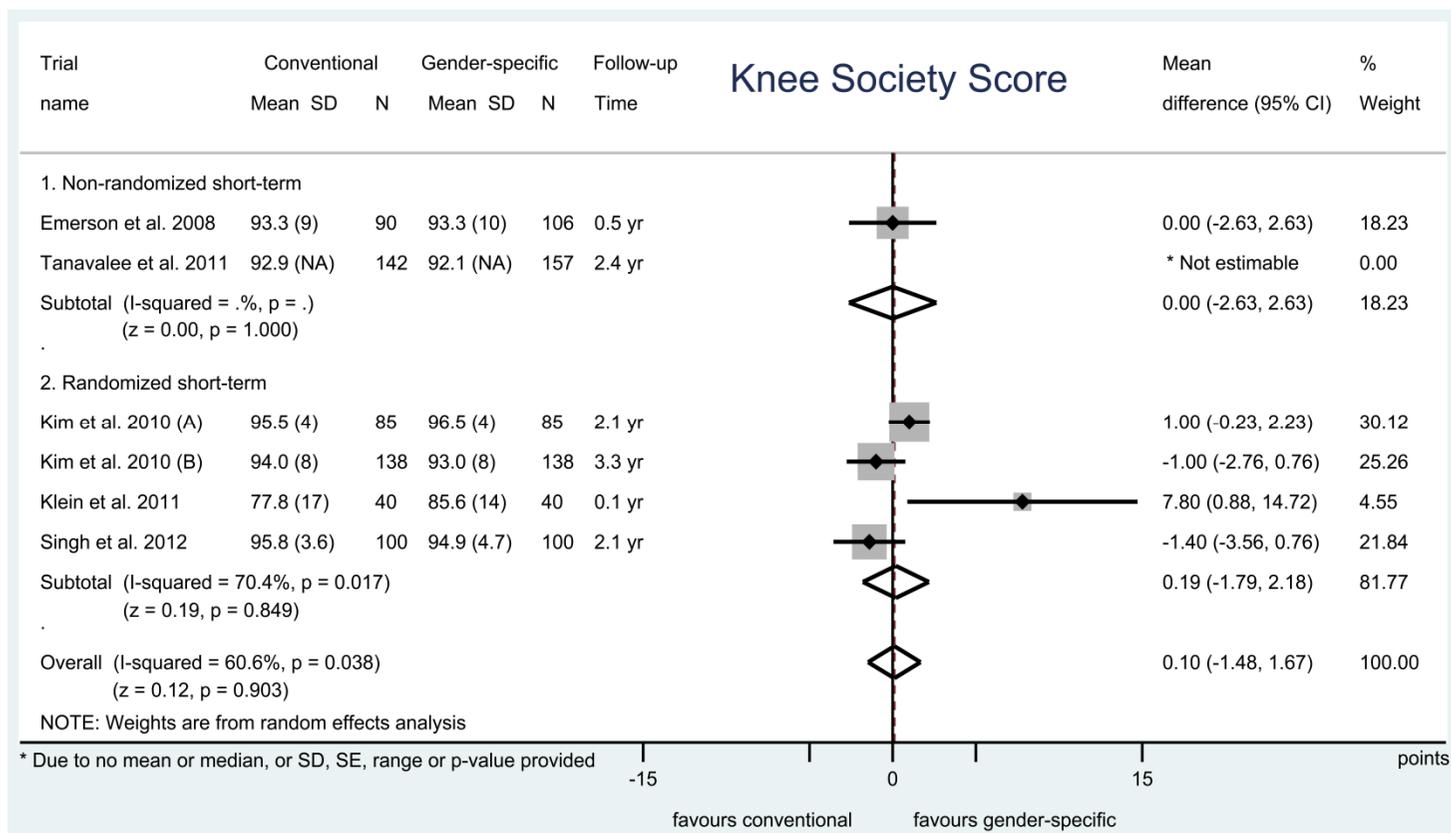
2012	to high		(16.6)	(13.5)			(14.9)	(15.1)					
		Postoperative	124.0	121.4	NA	NA	32.,6	31.6	NA	NA	10	7	63
			(14.8)	(17.0)			(9.2)	(8.5)			(20%)	(14%)	(66%)
Tanavalee, 2011	low	Preoperative	126.0	125.6	34.3	34.7	NA	NA	NA	NA	NA	NA	NA
		Postoperative	134.1	133.5	92.1	92.9	NA	NA	NA	NA	NA	NA	NA
Thomsen, 2012	Moderate to high	Preoperative	124 (90-140)	126 (110-140)	NA	NA	NA	NA	NA	NA	NA	NA	NA
		Postoperative	131 (108-150)	132 (105-147)	NA	NA	NA	NA	8	9	NA	NA	NA

NA = not available (not applicable or not provided), * significant difference

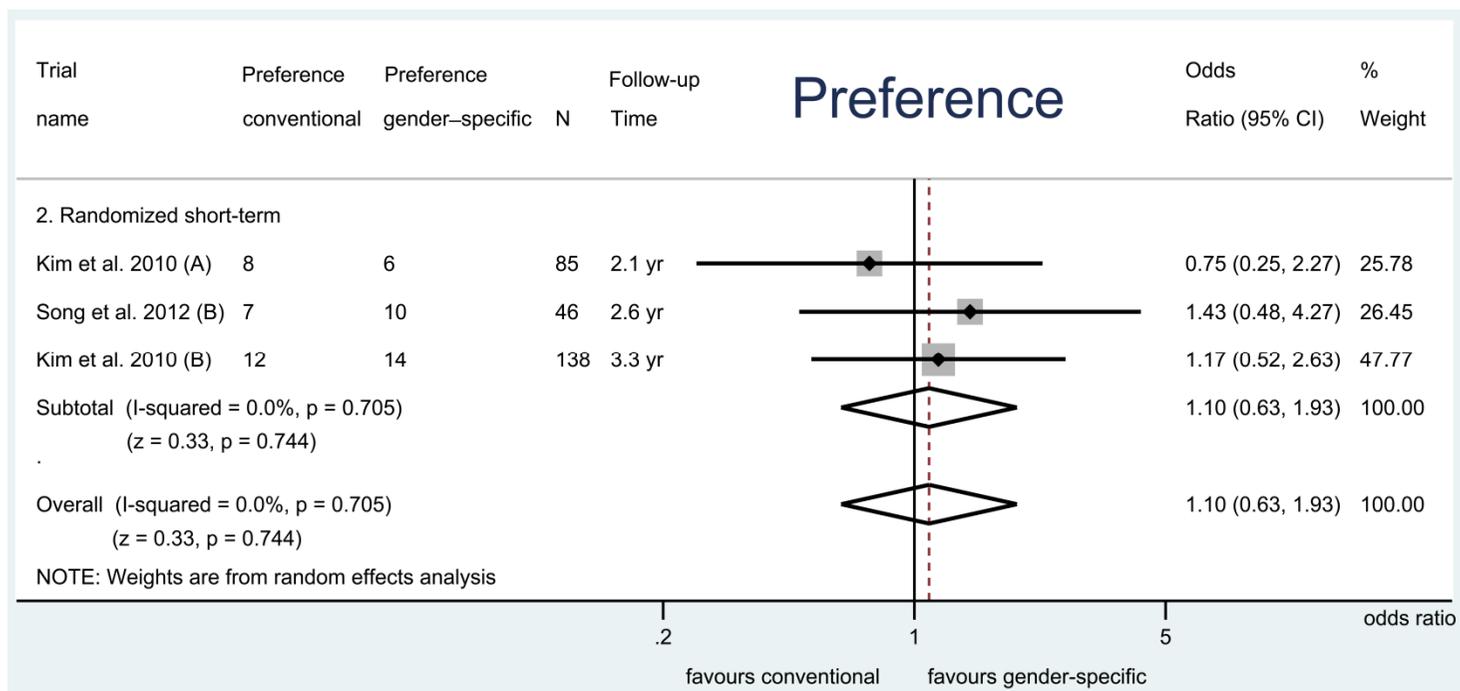
Forest plot for flexion-extension range of motion (in degrees) after short-term follow-up (intra-operative – 3.2 years):



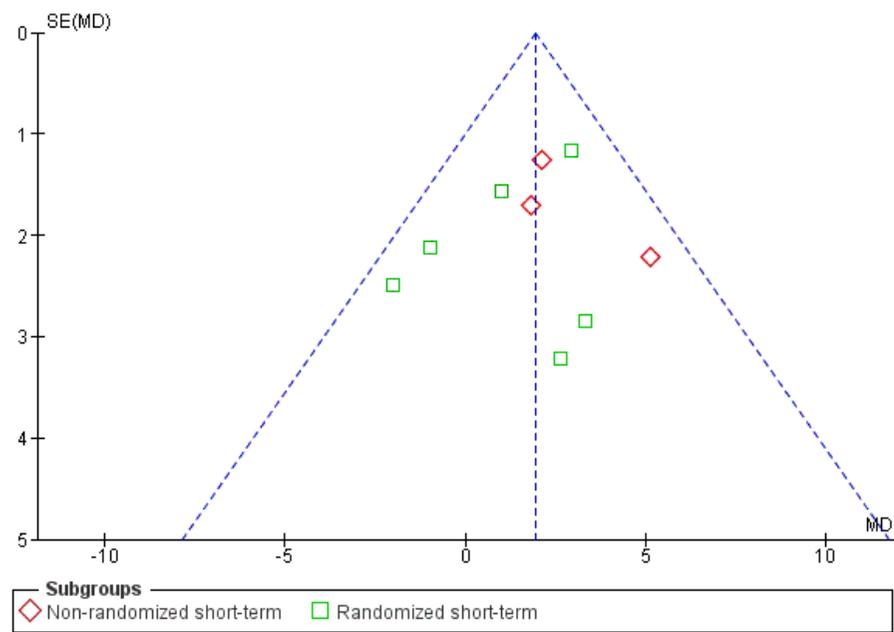
Forest plot for Knee Society Score (in points) after short-term follow-up (0.1 – 3.3 years):



Forest plot for component preference in patients with bilateral TKR after short-term follow-up (0.1 – 3.3 years):



Funnel plot for all 10 study cohorts



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